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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PATENT DEPARTMENT
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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 06/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,522	LAL ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this c mmunication appears on th c ver sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,12,30-45 and 56* is/are pending in the application.

4a) Of the above claim(s) *1,12,30,33,35,36,39,44,45 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,31,32,34,37,38 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 and 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1, 11, 12, 30-45, and 56 are pending in the instant application.

Applicants' election **with** traverse of Group II, claims 11, 31, 32, 34, 37, 38, and 40-43 in Paper No. 8, filed 03/22/02, is acknowledged.

It is noted that applicants request amendment to the specification at page 1 of Paper No. 8. However, there appears to be no amendment to the specification present in Paper No. 8.

Election/Restriction

1. Applicants traverse the restriction on the grounds that the claims of Groups IV-VI, drawn to methods of use or methods of making the antibody of Group II, should be rejoined. Applicants' argument has been fully considered but is not found persuasive. If the claims of Group II are found to be allowable, then the claims of Groups IV-VI will be evaluated to determine if they are directed to processes of making or processes of using the patentable product, and if so would be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also MPEP 821.04, In re Ochiai, and In re Brouwer). However, as the elected claims are not yet allowable, rejoinder is not as yet required.

Applicants further traverse on the grounds that co-examination of the claims of elected Group II with the claims of Groups I and III would not result in an undue burden on the examiner as the claims of Groups I and III are related to claims allowed in parent applications. Applicants' argument has been fully considered but is not found persuasive. A search for antibodies that bind a polypeptide not only includes an extensive search of the polypeptide sequence, but also includes an extensive search of antibodies that bind similar polypeptides to assess their ability to bind the claimed polypeptide and thus act as an antibody to the claimed polypeptide. While the search for polynucleotides will overlap with portions of the searches for encoded polypeptides and antibodies to said polypeptides, clearly the searches for polypeptides and antibodies are much more extensive resulting in a search burden on the examiner to

search all three patentably distinct inventions. Thus, a serious burden would be required for the examiner to search not only the polynucleotide sequences and encoded polypeptides, but also the antibodies that bind the encoded polypeptides.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 12, 30, 33, 35, 36, 39, 44, 45, and 56 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 8.

Specification/Informalities

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Antibody Against Human Sodium-Dependent Phosphate Cotransporter". See MPEP § 606.01.

Claim Objections

3. Claims 37, 38, 40, and 41 are objected to as being dependent upon a non-elected claim. It is suggested that applicants amend claims 37 and 40 to incorporate the limitations of claim 36 into claim 37 and to incorporate the limitations of claim 39 into claim 40.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 11, 31, 32, 34, 37, 38, and 40-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 11, 37, and 40 are drawn to antibodies that bind SEQ ID NO:1 or a biologically active fragment or immunogenic fragment thereof or a naturally-occurring amino acid sequence that is 90 %

identical to SEQ ID NO:1. Claims 31, 42, and 43 further limit the antibody of claim 11. Claims 32, 34, 38, and 41 are drawn to compositions comprising the antibodies of claims 11, 37, or 40. Applicants assert at least one utility for the claimed isolated antibody as useful in the purification of the polypeptide of SEQ ID NO:1 (page 42 of the instant specification). The specification also provides a general list of therapeutic (pages 23-30 of the instant specification) and diagnostic (pages 30-35 of the instant specification) uses for an antibody that binds the polypeptide of SEQ ID NO:1. However, the specification provides no specific and substantial utility for the polypeptide of SEQ ID NO:1 or any information linking the polypeptide of SEQ ID NO:1 to any **specific** disease state that could be treated or diagnosed using the claimed antibody. Thus, the asserted utility of the claimed antibody and compositions thereof as encompassed by the claims is not substantial or specific.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 11, 31, 32, 34, 42, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 11 (claims 31, 32, 34, 42, and 43 dependent thereon) is indefinite in the recitation of "biologically active." The specification discloses the meaning of this term as "having structural, regulatory, or biochemical functions of a naturally occurring molecule" (pages 5-6 of the instant specification). However, the scope of things encompassed by this "definition" is vague and it is unclear from the definition of this term what functions of SEQ ID NO:1 applicants intend as the meaning of "biologically active". It is suggested that the term "biologically active" be replaced with a term that clearly defines applicants' intended function(s).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 11, 31, 32, 34, 37, 38, and 40-43 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 11, 31, 32, 34, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 11 (claims 31, 32, 34, 42, and 43 dependent thereon) is rejected because the claim is drawn to a genus of antibodies that bind: a genus of polypeptides *comprising* SEQ ID NO:1 and a genus of polypeptides *comprising* a genus of naturally-occurring amino acid sequences at least 90% identical to SEQ ID NO:1 that have not been fully described in the specification. No description has been provided of the genus of polypeptide sequences and compositions encompassed by the claims. No information, beyond the characterization of SEQ ID NO:1 has been provided by applicants which would indicate that they had possession of the claimed genus of antibodies. The specification does not contain any disclosure of the function of all the naturally-occurring polypeptide sequences that are at least 90 % identical to SEQ ID NO:1 within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions and with the potentiality of generating many different antibodies. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. Furthermore, the specification does not contain any disclosure of the structure all polypeptide sequences *comprising* SEQ ID NO:1 or *comprising* a naturally-

occurring sequence that is at least 90 % identical to SEQ ID NO:1. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus, i.e., an antibody that specifically binds SEQ ID NO:1. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

9. Even if applicants demonstrate that the antibody and compositions thereof of specific for SEQ ID NO:1 have a specific and substantial utility, the following rejection still applies. Claims 11, 31, 32, 34, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that specifically binds the polypeptide of SEQ ID NO:1, does not reasonably provide enablement for an antibody that specifically binds: *any* polypeptide *comprising* the polypeptide of SEQ ID NO:1 or *any* polypeptide comprising an amino acid sequence having at least 90 % identity to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 11 (claim 31, 32, 34, 42, and 43 dependent thereon) is so broad as to encompass an antibody that specifically binds: *any* polypeptide *comprising* the polypeptide of SEQ ID NO:1 or *any* polypeptide *comprising* an amino acid sequence having at least 90 % identity to SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of antibodies broadly encompassed by the claims. Since the amino acid sequence of a protein determines the antibody elicited thereby, predictability of which changes can be tolerated in a protein's amino acid sequence and retain the desired antibody binding affinity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence comprise the antibody binding region or epitope. In the instant case, the disclosure is limited to an antibody that specifically binds the polypeptide of SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of an antibody binding target, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made

with a reasonable expectation of success in retaining the desired antibody binding are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass an antibody that specifically binds: any polypeptide *comprising* the polypeptide of SEQ ID NO:1, *any* polypeptide having at least 90 % identity to SEQ ID NO:1 because the specification fails to teach how to make and use an antibody that binds any polypeptide *comprising* SEQ ID NO:1 as the claim, as written, does not require the antibody to specifically bind SEQ ID NO:1, but allows for an antibody that is specific for amino acid sequence other than SEQ ID NO:1 that *comprises* the polypeptide. Furthermore, the specificity of an antibody is dependent on the structure of the polypeptide from which it was produced. Therefore, an antibody that binds an epitope within a specific sequence, e.g., the polypeptide of SEQ ID NO:1, will not necessarily bind a polypeptide that shares at least 90 % identity to SEQ ID NO:1 because the epitope may not be present in a polypeptide with at least 90 % identity to SEQ ID NO:1.

Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including an antibody that specifically binds: *any* polypeptide *comprising* the polypeptide of SEQ ID NO:1 or *any* polypeptide *comprising* an amino acid sequence having at least 90 % identity to SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 11, 32, 34, 37, 38, 40, and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Feder et al. (IDS reference; US Patent 5,872,237). Claims 11, 37, and 40 are drawn to antibodies that bind SEQ ID NO:1 or a biologically active fragment or immunogenic fragment thereof or a naturally-occurring amino acid sequence that is 90 % identical to SEQ ID NO:1. Claims 32, 34, 38, and 41 are drawn to compositions comprising the antibodies of claims 11, 37, or 40.

Feder et al. (hereafter referred to as "Feder") teaches a human polypeptide, SEQ ID NO:11, that is 96 % identical to the polypeptide of SEQ ID NO:1 of the instant application. The polypeptide of Feder is 100 % identical to amino acids 1-11, 13-94, 96-159, and 161-401 of SEQ ID NO:1 of the instant application. US Patent 5,872,237 teaches methods of generating monolclonal and polyclonal antibodies immunoreactive with the disclosed polypeptide of Feder. Feder teaches the antibodies produced by the disclosed methods can be labeled for use in immunoassays (column 16). This anticipates claims 11, 32, 34, 37, 38, 40, and 41 as written.

11. Claims 11, 32, 37, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Dillner et al. (WO 91/18294). Claims 11, 32, 37, and 38 are described above.

Dillner et al. (hereafter referred to as "Dillner") teaches a peptide having the sequence "PETTDLYCYEQLNDSSEEED" (page 38, line 24). Amino acids 11-17 of the peptide of Dillner are 100 % identical to amino acids 56-62 of the polypeptide of SEQ ID NO:1 of the instant application. Dillner discloses their peptide is an immunoreactive region of human papilloma virus (HPV). Dillner teaches a polyclonal antibody generated in guinea pigs and a method of producing said antibody (page 8). Dillner

discloses the use of their antibody for the detection of HPV. This anticipates claims 11, 32, 37, and 38 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 31, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feder in view of Krebber et al. (US Patent 5,514,548). Claims 31, 42, and 43 further limit the antibody of claim 11.

Feder discloses the teachings as described above. Feder does not teach an antibody of the type recited in claim 31 or an antibody generated by screening a Fab expression library or screening a recombinant immunoglobulin library.

Krebber et al. (hereafter referred to as "Krebber") teach the use of recombinant techniques for generating antibodies for specific uses and provide examples of such antibodies as chimeric and humanized antibodies (column 1). Krebber teaches a method of isolating high affinity antibodies by screening a library of recombinantly expressed ligand binding proteins such as a single chain Fv or Fab antibody fragment (columns 3 and 4). Krebber teaches this method facilitates isolation and provides improved binding affinity of an antibody to a target protein. Krebber teaches recombinant processes can produce antibodies better suited for human therapeutic applications than their murine progenitors by altering antigenic portions recognized by the human immune system (column 1).

Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art for an antibody against the polypeptide of Feder produced by the method of Krebber. One would have been motivated for such an antibody in order to reduce antigenicity of the antibody for human therapeutic use and/or to facilitate isolation and improve antibody binding as taught by Krebber.

One would have a reasonable expectation of success for an antibody against the polypeptide of Feder produced by the method of Krebber because of the results of Feder and Krebber. Therefore, claims 31, 42, and 43, drawn to the antibody of claim 11 of the type recited in claim 31 or the antibody of claim 11 generated by screening a Fab expression library or screening a recombinant immunoglobulin library, would have been obvious to one of ordinary skill in the art.

13. Claims 31, 34, and 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dillner in view of Krebber. Claims 31, 34, and 40-43 are described above.

Dillner discloses the teachings as described above. Dillner does not teach a monoclonal antibody or composition thereof to their disclosed peptide, an antibody of the type recited in claim 31 or an antibody generated by screening a Fab expression library or screening a recombinant immunoglobulin library.

Krebber et al. (hereafter referred to as "Krebber") teach the use of recombinant techniques for generating antibodies for specific uses and provide examples of such antibodies as chimeric and humanized antibodies (column 1). Krebber teaches a method of isolating high affinity antibodies by screening a library of recombinantly expressed ligand binding proteins such as a single chain Fv or Fab antibody fragment (columns 3 and 4). Krebber teaches this method facilitates isolation and provides improved binding affinity of an antibody to a target protein. Krebber teaches recombinant processes can produce antibodies better suited for human therapeutic applications than their murine progenitors by altering antigenic portions recognized by the human immune system (column 1).

Also, at the time of the invention, one of ordinary skill in the art would have known methods of generating a monoclonal antibody given a target antigen.

Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art for a monoclonal antibody against the peptide of Dillner or an antibody against the peptide of Dillner produced by the method of Krebber. One would have been motivated for a monoclonal antibody against the peptide of Dillner in order to provide more consistent results in the detection of HPV as a monoclonal antibody is specific for a single antigen rather than multiple antigens on a single peptide.

One would have been motivated for an antibody to the peptide of Dillner produced by the method of Krebber in order to improve antibody binding as taught by Krebber, thereby increasing detection limits of the immunoassay for HPV as taught by Dillner. One would have a reasonable expectation of success for a monoclonal antibody or an antibody against the polypeptide of Dillner produced by the method of Krebber because of the results of Dillner, Krebber, and the ability of one of ordinary skill in the art to generate a monoclonal antibody. Therefore, claims 31, 34, and 40-43, drawn to the antibodies and compositions thereof as described above, would have been obvious to one of ordinary skill in the art.

Conclusion

14. All claims are rejected. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Art Unit is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

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ELIZABETH SLOBODYANSKY, PH.D
PRIMARY EXAMINER